

U.S.S.N. 10/015,930  
Filed: November 30, 2001  
RESPONSE TO OFFICE ACTION

**In the Claims**

AH 1. (Amended) A pharmaceutical composition in unit dosage form for both intraoral and oral administration to a patient, ~~said unit dosage form configured to be placed intraorally in said patient~~, which comprises:

- (a) an intraorally releasing ~~as a first releasing~~ portion, in the form of a molded triturate tablet comprising a therapeutically effective amount of at least one pharmaceutically active ingredient capable of intraoral administration; and
- (b) as a second releasing portion located around the first portion as a compressed annular tablet, comprising a therapeutically therapeutic ingredient capable of oral administration and which is releasable and orally ingestible by the patient after the molded triturate has disintegrated or has dissolved intraorally.

2. The pharmaceutical composition defined in claim 1 in the form of a compressed annular tablet and a molded triturate tablet.

3. The pharmaceutical composition defined in claim 1 wherein the compressed annular tablet is comprised of one or more layers containing the pharmaceutically active ingredient capable of oral administration.

4. The pharmaceutical composition defined in claim 1 wherein the molded triturate tablet contains a therapeutically effective amount of at least one pharmaceutically active ingredient capable of intraoral administration and one or more pharmaceutically acceptable excipients for intraoral administration.

5. The pharmaceutical composition defined in claim 2 wherein the molded triturate tablet is formulated with a pharmaceutically acceptable effervescent agent capable of generating effervescence when contacted with saliva.

U.S.S.N. 10/015,930

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**RESPONSE TO OFFICE ACTION**

6. The pharmaceutical composition as defined in claim 1 where the compressed annular tablet may be film coated and may contain a pharmaceutically acceptable flavoring agent.

7. The pharmaceutical composition defined in claim 3 wherein the compressed annular tablet is an immediate drug release tablet comprising at least one pharmaceutically active ingredient capable of oral administration and one or more pharmaceutically acceptable excipients for oral administration.

8. The pharmaceutical composition defined in claim 3 wherein the compressed annular tablet comprises more than one layer including a sustained release layer containing a therapeutically effective amount of a first pharmaceutically active ingredient capable of oral administration and optionally including an immediate release layer containing a therapeutically effective amount of a second pharmaceutically active ingredient capable of oral administration, same or different from the first.

9. The pharmaceutical composition defined in claim 3 wherein the compressed annular tablet comprises more than one layer comprising the pharmaceutically active ingredient capable of oral administration and where at least one of the layers comprising the pharmaceutically active ingredient capable of oral administration is an immediate drug release layer.

10. The pharmaceutical composition defined in claim 8 where the compressed annular tablet provides sustained release of the pharmaceutical active ingredient capable of oral administration for a period of 0.5 to 24 hours.

U.S.S.N. 10/015,930  
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11. The pharmaceutical composition defined in claim 10 wherein the compressed annular tablet is formulated by incorporating or coating the pharmaceutically active ingredient with one or more pharmaceutically acceptable sustained released polymers.

12. The pharmaceutical composition defined in claim 11 wherein the one or more pharmaceutically acceptable sustained release polymer is selected from the group consisting of methylcellulose, hydroxypropyl methylcellulose, ethyl cellulose, cellulose acetate phthalate, acacia, gums, wax, glycerol monostearate, acrylic acid polymers and copolymers, methacrylic acid, methyl acrylate, ethyl acrylate, methyl methacrylate, ethyl methacrylate, and ion exchange resins capable of forming a sustained release ion-exchange resin-drug complex.

13. The pharmaceutical composition defined in claim 3 wherein the compressed annular tablet comprises a therapeutically effective amount of one or more pharmaceutically active ingredients capable of oral administration in a delayed release form which delays the release of the one or more pharmaceutically active ingredients capable of oral administration for a period of 0.5 to 12 hours.

14. The pharmaceutical composition defined in claim 13 wherein the compressed annular tablet comprising a therapeutically effective amount of one or more pharmaceutically active ingredients capable of oral administration in a delayed release form includes a delayed release coating on the one or more pharmaceutically active ingredients, said delayed release coating comprising one or more pharmaceutically acceptable polymers selected from the group consisting of methylcellulose, hydroxypropyl methylcellulose, hydroxyethyl cellulose, hydroxymethyl cellulose, hydroxypropyl cellulose acetate succinate, ethyl cellulose, cellulose acetate phthalate,

U.S.S.N. 10/015,930

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**RESPONSE TO OFFICE ACTION**

cellulose acetate trimellitate, carboxymethylcellulose sodium, acrylic acid polymers and copolymers, polymers or copolymers of methacrylic acid, methyl acrylate, ethyl acrylate, methyl methacrylate, ethyl methacrylate, vinyl acetate, vinyl acetate phthalate, an azo compound, polyvinyl pyrrolidone, pectin amylose, shelac, zein and guar gum.

15. The pharmaceutical composition defined in claim 3 wherein the compressed annular tablet is chewable and comprises one or more pharmaceutically acceptable excipients suitable for a chewable medication and a flavoring agent.

16. The pharmaceutical composition defined in claim 1 wherein the molded triturate tablet disintegrates or dissolves within 10 minutes permitting rapid release of the pharmaceutically active ingredient capable of intraoral administration, when the composition is contacted with saliva during intraoral administration.

17. The pharmaceutical composition defined in claim 1 wherein the compressed annular tablet containing the pharmaceutically active ingredient capable of oral administration remains substantially intact until the intraoral administration of the pharmaceutically active ingredient capable of intraoral administration has been completed.

18. The pharmaceutical composition defined in claim 1 wherein the pharmaceutically active ingredient capable of intraoral administration has a rapid onset of the desired therapeutic effect through intraoral absorption.

19. The pharmaceutical composition defined in claim 1 wherein the pharmaceutically active ingredient capable of intraoral administration is selected from the group consisting of analgesics, antihistamines, antidiarrheal, anxiolytic, hypnotics, stimulants, cardiovascular drugs, pulmonary drugs, antihypertensives, antiemetics, anti-

U.S.S.N. 10/015,930  
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inflammatory drugs, renal drugs, steroids, drugs for neurological disorders, anti-psychotic drugs, drugs for treating endocrine disorders, drugs for promoting immunology, drugs for treating osteoarthritis, drugs for treating glaucoma, drugs for treating allergic rhinitis, drugs for treating anemias and other hematological disorders, drugs for treating infectious diseases, drugs for the treatment and symptoms of cancer, drugs for insomnia, and antidiabetic drugs.

20. A process for the preparation of a pharmaceutical composition in unit dosage form as a compressed annular tablet with molded triturate tablet for both intraoral and oral administration to a patient, said pharmaceutical composition to be placed intraorally of said patient, which comprises:

(a) as a first releasing portion, a molded triturate tablet comprising a therapeutically effective amount of at least one pharmaceutically active ingredient capable of intraoral administration; and

(b) as a second releasing portion located around said first portion, a therapeutically effective amount of at least one pharmaceutically active ingredient capable of oral administration and which is releasable and orally ingestible by the patient after the inlaid triturate has disintegrated or has dissolved intraorally,

which comprises the steps of:

(i) providing the second portion as a single- or multi-layer compressed annular tablet, and

(ii) molding the first portion as a triturate tablet into the annulus of (i).

U.S.S.N. 10/015,930  
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**RESPONSE TO OFFICE ACTION**

21. A method of administering a pharmaceutical composition in unit dosage form as a compressed annular tablet molded triturate tablet for both intraoral and oral administration to a patient, which comprises:

(a) as a first releasing portion, a molded triturate tablet comprising a therapeutically effective amount of at least one pharmaceutically active ingredient capable of intraoral administration; and

(b) as a second releasing portion located around the said first portion, a therapeutically effective amount of at least one pharmaceutically active ingredient capable of oral administration and which is releasable and orally ingestible by the patient after the inlaid triturate has disintegrated or has dissolved intraorally, which comprises the steps of:

(i) placing the pharmaceutical composition under the tongue or against the inner wall of the cheek or within the vestibular mucosa of said patient;

(ii) retaining the pharmaceutical composition under the tongue or against the inner wall of the cheek or vestibular mucosa of the patient until the first releasing portion of the pharmaceutical composition containing the pharmaceutically active ingredient capable of intraoral administration has dissolved or has disintegrated thereby substantially releasing the pharmaceutically active ingredient capable of intraoral administration; and

(iii) following step (ii) sucking or swallowing whole or chewing and swallowing the second releasing portion of the pharmaceutical composition.

22. The pharmaceutical composition defined in claim 1 wherein the pharmaceutically active ingredient capable of intraoral administration has a first pass metabolism which is avoided by intraoral administration.

U.S.S.N. 10/015,930

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**RESPONSE TO OFFICE ACTION**

23. The pharmaceutical composition defined in claim 1 wherein the pharmaceutically active ingredient capable of intraoral administration has a rapid onset of desired therapeutic effect through intraoral absorption.